Sulfenamide Accelerators Category – Comments of Environmental Defense

(Submitted via Internet 4/25/02)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Sulfenamide Accelerators Category CAS Nos. 102-77-2; 13752-51-7 (+ chemicals 95-31-8; 95-33-0; 4979-32-2 for data purposes).

The robust summary/test plan submitted by the American Chemistry Council's Rubber and Plastic Panel (RAPA) provides an extensive compilation of data addressing most testing requirements for High Production Volume Chemicals. We complement RAPA on their extensive review and well-organized presentation of the literature. We also appreciate the description of uses, structural characteristics of the category, chemical/physical properties and other discussion of these and structurally related chemicals in the Justification and Testing Rationale.

The extent of the data provided in the robust summary demonstrates that these chemicals have been the subjects of extensive previous testing. We note, however, that data gaps exist for biodegredation and developmental toxicity for N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide. Comparison of data presented for chemicals of similar structure indicate that biodegradation of this chemical would be minimal. Thus, we would consider extrapolation of that observation to predict minimal biodegradation of this compound to be acceptable.

The lack of data describing developmental toxicity is of greater concern. That is, the chemical structure of N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide differs sufficiently from other chemicals described, and the relevance of developmental toxicity is so great, that studies of developmental toxicity of this compound should be required in our view.

Other comments:

N-oxydiethylene benzothiazole 2-sulfenamide

1. Data presented for acute toxicity of N-oxydiethylene benzothiazole 2-sulfenamide and similar compounds are variable, but indicate this compound has low toxicity when administered orally or dermally at high doses. It is significantly more toxic when administered by intra-peritoneal injection. Further, in repeat dose studies the LOAEL for this compound was relatively low, 50 mg/kg. These observations indicate that N-oxydiethylene benzothiazole 2-sulfenamide is not well absorbed from the gastrointestinal tract or skin when administered in large doses. It appears, however, that a much higher percent of lower doses is absorbed is absorbed from the gastrointestinal tract. Thus, LD50 data generated with a single dose administered orally or applied to the skin that indicate low acute toxicity may be misleading when extrapolated to predict risk associated with repeated low dose exposure. That is, these data do not accurately reflect risk associated with repeated or chronic exposure such as could occur in the occupational settings.

2. Although the data compilation for N-oxydiethylene benzothiazole 2-sulfenamide is very thorough, some of the studies included are not complete, poorly described, or are otherwise not valid. While it may be appropriate to include such studies to indicate that they have not been inadvertently overlooked, it would seem desirable to note that they are not being relied upon. This is especially true when valid studies conducted under GLP are available.

N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide

1. As observed above for N-oxydiethylene benzothiazole 2-sulfenamide, it appears that N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide and other chemicals in the group are poorly absorbed from the gastrointestinal tract and skin. Thus, data for acute toxicity based on single large doses may be

misleading as indicated by the fact that doses as low as 600 ppm in the diet induced both toxicity and increased tumor rates when administered chronically. In other studies doses as low as 200 ppm resulted in lower body weights.

2. As mentioned above the structure of N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide differs significantly from other chemicals described in this package. Biological significance of these structural differences is seen in the fact that N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide was a positive carcinogen at 600 ppm whereas studies of two other compounds in this group were negative. Further, other chemicals in this package appear to exhibit some developmental toxicity at doses as low as 400 mg/kg or lower. Thus, we do not considered it appropriate to extrapolate data from other chemicals described in this report to predict risks to developmental toxicity that might be associated with N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide.

In conclusion we feel that RAPA and its member companies have done a good job of compiling data for sulfenamide accelerators. The data are extensive. It is unfortunate that more of these studies have not been published in the open literature. Data described are thorough and complete except for a study of the developmental toxicity of N-oxydiethylene thiocarbamoyl-N'-oxydiethyllene sulfenamide. It is our opinion that such studies should be required.

Thank you for this opportunity to comment.

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